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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

10/10/99

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 03/10/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<p align="center">Office Action Summary</p>	<p>Application No.</p> <p>09/442,898</p>	<p>Applicant(s)</p> <p>AGUET, MICHAEL</p>	
	<p>Examiner</p> <p>Gary B. Nickol Ph.D.</p>	<p>Art Unit</p> <p>1642</p>	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 January 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- | | |
|---|--|
| 15) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s) _____ |
| 16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 17) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3,4</u> | 20) <input type="checkbox"/> Other: |

DETAILED ACTION

The response filed on January 5, 2001 (Paper No. 7) to the restriction requirement of December 05, 2000 has been received. Applicant has elected Group I, claims 1-6 for examination without traverse. Claims 7-22 were cancelled. Thus, claims 1-6 are pending and are currently under examination.

Oath/Declaration

The oath or declaration is defective because it has not been signed by the inventor.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4,6 are rejected under 35 U.S.C. 102(b) as being anticipated by Caras et al. (WO 96/13518, May 1996).

The claims are drawn to a method of inhibiting angiogenesis in a mammal comprising administering to the mammal an amount of an Eph receptor antagonist which is effective for inhibiting angiogenesis in the mammal (Claim 1); wherein the mammal is a human (Claim 2); wherein the antagonist binds an Eph receptor (Claim 3); wherein the antagonist is an antibody (Claim 4); wherein the mammal is suffering from a disease or disorder characterized by undesirable or excessive vascularization or vascular permeability (Claim 6).

Caras et al teach a method of inhibiting angiogenesis in a mammal comprising administering to the mammal an amount of an Eph receptor antagonist which is effective for

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inhibiting angiogenesis in the mammal wherein the mammal is suffering from a disease or disorder characterized by undesirable or excessive vascularization or vascular permeability (abstract, and pages 29-30); wherein the mammal is a human (page 28, line 1); wherein the antagonist binds an Eph receptor and the antagonist is an antibody (page 23, lines 22-32).

Claims 1,4 are further rejected under 35 U.S.C. 102(b) as being anticipated by Pandey et al. (Science, Vol. 268, April 1995, IDS).

Pandey et al. teach a method of inhibiting angiogenesis in a mammal comprising administering to the mammal an amount of an Eph receptor antagonist which is effective for inhibiting angiogenesis in the mammal wherein the antagonist binds is an antibody (abstract, and page 568, 3rd column, 1st paragraph, also Figure 4).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caras (WO 96/13518, May 1996) in view of Wang et al. (Cell, Vol. 93, pages 741-753, May 29, 1998, IDS).

The claims are drawn to a method of inhibiting angiogenesis in a mammal comprising administering to the mammal an amount of an Eph receptor antagonist which is effective for

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inhibiting angiogenesis in the mammal (Claim 1); wherein the mammal is a human (Claim 2); wherein the antagonist binds an Eph receptor (Claim 3); wherein the antagonist is an antibody (Claim 4); wherein the antibody binds EphB4 receptor (Claim 5); wherein the mammal is suffering from a disease or disorder characterized by undesirable or excessive vascularization or vascular permeability (Claim 6).

1. Caras teaches as set forth above.
2. Caras does not include an antibody which binds the EphB4 receptor.
3. Wang et al. teach the disruption between the EphB4 receptor and its ligand, ephrin-B2, prevents the remodeling of veins and disrupts arterial remodeling (page 741, 2nd column, 3rd paragraph), and that ephrin-B2-mediated interactions are essential for angiogenesis (page 749).

I It would have been *prima facie* obvious to one of ordinary skill in the art to modulate the method of Caras et al. so as to include an antibody which binds the EphB4 receptor in view of the teachings of Wang et al. because Wang et al. teach that disruption between the EphB4 receptor and its ligand, ephrin-B2, prevents the remodeling of veins and disrupts arterial remodeling. One would have been motivated to do so because it was well known in the art at the time the invention was made that Eph receptors comprise two families- A class receptors and B-class receptors and that Eph-A-class receptors and their ligands are implicated in angiogenesis (Wang et al. , page 749). Thus, it would have been obvious to modulate the method of Caras et al. so as to prevent angiogenesis by further including an antibody against the B-class receptors so as to prevent its ligand (ephrin-B2) from interacting with the EphB4 receptor.

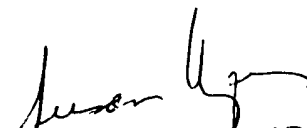
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
March 5, 2001


SUSAN UNGAR, PH.D.
PRIMARY EXAMINER